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09/785,657	02/20/2001	Ulf Landegren	LANDEGREN=1A	5356

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EXAMINER

CHUNDURU, SURYAPRABHA

ART UNIT	PAPER NUMBER
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1637

DATE MAILED: 09/12/2002

13

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/785,657

Applicant(s)

LANDEGREN ET AL.

Examiner

Suryaprabha Chunduru

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 27 June 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-7, 13-15 and 17-24 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7, 13-15 and 17-24 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_ 6) ☐ Other: \_\_\_\_\_

**DETAILED ACTION**

1. Applicants' response to the office action and amendment (Paper No.12) filed on June 27, 2002 has been entered.

**Response to Arguments**

2. Applicant's response to the office action (Paper No.12) is fully considered and deemed persuasive in part.

3. The rejection made under 35 U.S.C. 112 second paragraph in the previous office action is withdrawn herein in view of the applicants' amendment (Paper No.12).

4. The following rejection was made in the previous office action under 35 U.S.C. 102(b):

a. Claims 1-7, and 13-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Landgren (WO 97/00446).

Landgren teaches a method for detecting analyte(s) in a solution, wherein the method comprises binding of two or more proximity probes (oligonucleotides) to a respective binding site on the analyte, wherein the proximity probes are comprised of a binding moiety (interacting species modified with crosslinkable compounds such as lectins, receptors, antibodies, oligonucleotides) and allowing binding moiety to bind to the analyte (antibody-antigen) and the proximity probes interact with each other (oligonucleotides of neighbouring antibodies are conjugated to each other) and detecting the interaction between nucleic acids (oligonucleotides) (see page 3, paragraph 4, page 4, lines 1-8, 21-31). Landgren also teaches that the method comprises (i) amplification of the interacted nucleic acids and detection of amplified product (see page 4, lines 7-8,); binding moieties of the proximity probes selected from antibodies, lectin, receptors, nucleic acids (oligonucleotides) (see page 4, paragraph 5, and page 5, paragraph 5);

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detection of an unknown analyte in a solution, and screening ligand candidates (antibody-affinity reagents) (see page 6, paragraphs 1-3). Therefore the disclosure of Landegren meets the limitations in the instant claims.

**Response to Arguments**

Applicants' arguments with respect to the above rejection are fully considered and found not persuasive because First, Applicants' particular argument that the method as disclosed in prior art of the record depends on "immobilization on a solid support", which is not relevant with respect to the instant claims, since the instant claim 1 does not recite any non-dependency on solid support or immobilization of target-probe complex on solid support. So this limitation is NOT in the claim. Further the target-probe reaction as disclosed in the prior art is dependent on solution medium. Second, the claim is of the open "comprising" format, which permits the inclusion of additional elements, so that any addition of steps are permitted in the claim. The instant claims recite a detection step, which did not recite how detection is performed. Hence "comprising" format permits many other limitations and steps. Therefore the rejection is maintained herein.

5. The following rejection was made in the previous office action under 35 U.S.C. 102(b):

Claims 1,3-5, and 7, 14, and 17-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Landegren et al. (USPN. 4,988,617).

Landgren et al. teach a method for detecting analyte(s) (target nucleic acid) in a solution, wherein the method comprises binding of two or more proximity probes (oligonucleotides) to a respective binding site on the analyte, wherein the proximity probes are comprised of a binding moiety (biotin) and allowing binding moiety to bind to the analyte and the proximity probes

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interact with each other (adjacent oligonucleotide probes join each other) and detecting the interaction between nucleic acids (oligonucleotides) (see column 3, lines 1-38, column 4, lines 34-50, column 10, 48-60). Landgren et al. also teach that the method (i) comprises binding moieties of the proximity probes selected from antibodies, carbohydrate and complementary strands of DNA (see column 10, lines 60-67); (ii) can be used to detect infectious agents in a test substance (see column 4, lines 12-19). Therefore the disclosure of Landegren et al. meets the limitations in the instant claims.

**Response to Arguments:**

Applicant's arguments with respect to the rejection made under 35 U.S.C. 102(b) claims 1, 3-5, and 7, 14, and 17-18 have been considered and are found not persuasive. Applicants argue that the method claimed is distinct from the method in the prior art since the instant claims do not require immobilization of target-probe complex, which is the central step of the cited prior art. This argument is unavailing for two reasons. First, the limitation on which the arguments are based is not relevant with respect to the instant claims and the prior art references teach each of the limitations found in the claims and the immobilization step is not the central step in the prior art of the record. The prior art of the record teaches detection of binding moiety (biotin moiety) with streptavidin bound to a solid support. So it is not the central step of the invention in the prior art of the record. Second, the claim is of the open "comprising" format, which permits the inclusion of additional elements, so that any addition of steps are permitted in the claim. The instant claims recite a detection step, which did not recite how detection is performed. Hence as discussed above "comprising" format permits many other limitations and steps. Therefore the rejection is maintained herein.

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6. The following rejection was made in the previous office action under 35 U.S.C. 102(b):

Claims 1,3-5, 7, 14, and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Landegren et al. (USPN. 5,871,921).

Landgren et al. teach a method for detecting analyte(s) (target nucleic acid) in a solution, wherein the method comprises binding of two or more proximity probes (oligonucleotides) to a respective binding site on the analyte, wherein the proximity probes are comprised of a binding moiety (intermediate segments) and allowing binding moiety to bind to the analyte and the proximity probes interact with each other (adjacent oligonucleotide probes join each other interlocking target nucleic acid) and detecting the interaction between nucleic acids (oligonucleotides) (see columns 13-14, claims 1, 2,6-9, column 3, lines 25-57, 62-67). Landgren et al. also teaches that the method comprises binding moieties of the proximity probes selected from protein, polypeptide, carbohydrate and synthetic polymer (see column 14, lines 9-12 or claim 9); method can be used to screen DNA or RNA libraries (see column 4, lines 2-5). Therefore the disclosure of Landegren et al. meets the limitations in the instant claims.

**Response to Arguments:**

Applicant's arguments with respect to the rejection made under 35 U.S.C. 102(b) claims 1,3-5, and 7, 14, and 16 have been considered and are found not persuasive. Applicants argue that the method claimed is distinct from the method in the prior art. Applicants' particular argument that the "intermediate segments" should not be considered as binding moiety, is fully considered and found not persuasive because first, the limitation on which the arguments are based is not relevant with respect to the instant claims, and the prior art discloses that the intermediate segment comprises a detectable tag or label (see column 3, lines 51-57) and it is a part of the

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probe used in the said method wherein the probe binds with the target and once the probe is bound to the target it interacts with the proximity probe to form circularized structure, which is detectable using detection reagent. The claims are of the open "comprising" format, which permits the inclusion of additional elements, so that any addition of steps are permitted in the claim. Hence as discussed above "comprising" format permits many other limitations and steps. Therefore the rejection is maintained herein.

### **New Grounds of Rejection**

#### ***Claim Rejections - 35 USC § 112***

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

(i) Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 14 is indefinite over the recitation of "capable of interacting" because capability is a latent characteristic and the claims do not set forth the criteria by which to determine capability. That is, it is not clear whether the recited oligonucleotide have the potential to interact or do in fact do interact with the recited proximity probe. Amendment of the claim to read, for example, "which interacts" would obviate this rejection.

(ii) Claims 4 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 4 is confusing for referring to the subject matter in the term "and/or" and "is/are". Thus it is unclear how the claims can simultaneously encompass all of these limitations (protein(s) / prion(s) / nucleic acid(s)). The claim should refer to the subject

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matter in the alternative only, the replacement of the term "and/or" with "or" or the addition of dependent claims are suggested.

*Claim Rejections - 35 USC § 103*

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 1-8, 13, 17-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Landegren *et al.* (WO 97/00446) and in view of Royer *et al.* (USPN. 6,306,587).

Landgren teaches a method for detecting analyte(s) in a solution, wherein the method comprises binding of two or more proximity probes (oligonucleotides) to a respective binding site on the analyte, wherein the proximity probes are comprised of a binding moiety (interacting species modified with crosslinkable compounds such as lectins, receptors, antibodies, oligonucleotides) and allowing binding moiety to bind to the analyte (antibody-antigen) and the proximity probes interact with each other (oligonucleotides of neighbouring antibodies are

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conjugated to each other) and detecting the interaction between nucleic acids (oligonucleotides) (see page 3, paragraph 4, page 4, lines 1-8, 21-31). Landgren also teaches that the method comprises (i) amplification of the interacted nucleic acids and detection of amplified product (see page 4, lines 7-8,); binding moieties of the proximity probes selected from antibodies, lectin, receptors, nucleic acids (oligonucleotides) (see page 4, paragraph 5, and page 5, paragraph 5); detection of an unknown analyte in a solution, and screening ligand candidates (antibody-affinity reagents) (see page 6, paragraphs 1-3). However Landgren did not teach detection of infectious agents, and interaction of proximity probes through 3' and 5' orientation.

Royer et al. teach a method for detecting analyte(s) (target nucleic acid) in a solution, wherein Royer teach that (i) the method comprises detection of infectious agents in food or humans (see column 15, lines 52-57); (ii) the interaction of one probe at 3' end with 5, end of a second probe (see column 6, lines 61-67, column 7, lines 1-3).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method of detecting target nucleic acid as taught by Landegren with the method as taught by Royer et al. which is well known in the art at the time the invention was made, because Landgren states that "the invention is not restricted to detection of any special kind of macromolecule, such as antigen. Examples of macromolecules are human myoglobin and human growth hormone, of which growth hormone have significant value in clinical situations" (see page 6, paragraphs 2-3). One such alternative form of detecting macromolecules of clinical importance, expressly motivated by Royer et al. is the use proximity probe-target detection method to detect infectious agents. An ordinary practitioner would have been motivated to combine the method of Landegren with the method of Royer et al. in order to

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achieve the expected advantage of a rapid and sensitive method for detecting a target nucleic acid.


*Conclusion*

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 703-305-1004. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-0294 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

  
Suryaprabha Chunduru  
September 5, 2002

  
JEFFREY FREDMAN  
PRIMARY EXAMINER